



## APPENDIX C

### **SPECIFICATION SUPPORT FOR NEW CLAIMS 47 AND 48 IN USSN 09/724,869 ("the '869 Application)**

New Claims in '869 Application	Support in '869 Specification
47. A method for obtaining an immunomodulatory polynucleotide that has an optimized modulatory effect on an immune response as compared to the response prior to optimization, or encodes a polypeptide that has an optimized modulatory effect on an immune response as compared to the response prior to optimization, the method comprising:	Claim 47 is one alternative of the Count. Support can be found in the '869 application at least in the title, at p. 3, l. 30 to p. 5, l. 5 and original claims 1 and step (2) of original claim 5.
a) creating a library of recombinant polynucleotides; and	Support for step (a) can be found at least at p. 4, ll. 23-24 ("to produce a library of recombinant polynucleotides"); p. 11, ll. 3-11 and original claim 1.
b) screening the library to identify an optimized recombinant polynucleotide that has, or encodes a polypeptide that has, a modulatory effect on an immune response induced by a vector;	Support for step (b) can be found at least at p. 4, l. 24-27 ("screening the library to identify at least one optimized recombinant polynucleotide . . . to modulate an immune response. . . ."); p. 7, ll. 24 to p. 8, l. 9; and original claim 1.
wherein the optimized recombinant polynucleotide or the polypeptide encoded by the recombinant polynucleotide exhibits an enhanced ability to modulate an immune response compared to a polynucleotide from which the library was created;	Support for this clause can be located at least at p. 4, ll. 24-27 (see above) and claim 1 and step (2) of original claim 5.
wherein said optimized modulatory effect on an immune response is induced by a genetic vaccine vector,	Support for this clause can be located at least in original claim 1 (" . . . to identify an optimized recombinant polynucleotide that has, or encodes a polypeptide that has, a modulatory effect on an immune response induced by a genetic vaccine vector;").

<b>New Claims in '869 Application</b> wherein the optimized recombinant polynucleotide encodes a co-stimulator selected from B7-1 (CD80) or B7-2 (CD86) and the screening step involves selecting variants with altered activity through CD28 or CTLA-4,	<b>Support in '869 Specification</b> Support for this clause can be located at least at p. 4, ll. 6-8 (examples of polynucleotides encoding costimulators, including, e.g., B7-1 and B7-2); p. 5, l. 31 to p. 6, l. 8; p. 16, ll. 24-28; p. 39, ll. 14-19; p. 46, ll. 23-25; p. 49, l. 13 to p. 53, l. 20; p. 68, l. 23, Example 1; Figures 10; 11, and Figure 15; and original claims 24 ("the optimized recombinant polynucleotide encodes a costimulatory") and 25 ("screening step involves selecting variants with altered activity through CD28 or CTLA-4").
and whereby optimization is achieved by recursive sequence recombination.	Support can be located at least at p. 17, ll. 21-31 ("recursive sequence recombination can be employed to achieve still further improvements in a desired property" and "Recursive sequence recombination entails successive cycles of recombination to generate molecular diversity."); p. 18, ll. 18-30.
<b>48.</b> A method for obtaining an immunomodulatory polynucleotide that has an optimized modulatory effect on an immune response as compared to the response prior to optimization, or encodes a polypeptide that has an optimized modulatory effect on an immune response as compared to the response prior to optimization, the method comprising:	Claim 48 is one alternative of the Count. Support for this claim is the same as that for Claim 47, the only difference between the claims being the added recitation in claim 48 of the term "variant".
a) creating a library of recombinant polynucleotides; and	Supported as described for claim 47.
b) screening the library to identify an optimized recombinant polynucleotide that has, or encodes a polypeptide that has, a modulatory effect on an immune response induced by a vector;	Supported as described for claim 47.
wherein the optimized recombinant polynucleotide or the polypeptide encoded by the recombinant polynucleotide exhibits an enhanced ability to modulate an immune response compared to a polynucleotide from which the library was created;	Supported as described for claim 47.

New Claims in '869 Application	Support in '869 Specification
wherein said optimized modulatory effect on an immune response is induced by a genetic vaccine vector, wherein the optimized recombinant polynucleotide encodes a co-stimulator selected from a B7-1 (CD80) variant or a B7-2 (CD86) variant and the screening step involves selecting variants with altered activity through CD28 or CTLA-4,	Support for a B7-1 variant or a B7-2 variant can be found at least at p. 7, ll. 7-8, and p. 50, l. 28 to p. 53, l. 20 ("DNA shuffling or other recombination method is used to generate B7 (e.g., B7-1/CD80 and B7-2/CD86) variants which have altered relative capacity to act through CD28 and CTLA-4. . . ."); <i>see also</i> claim 47 above.
and whereby optimization is achieved by recursive sequence recombination.	Supported as described for claim 47.